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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,325	08/10/2001	Martin Gleave	UBC.P-020	8469
57381	7590	02/28/2007		
Marina Larson & Associates, LLC			EXAMINER	
P.O. BOX 4928			VIVLEMORE, TRACY ANN	
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			ART UNIT	PAPER NUMBER
			1635	
			MAIL DATE	DELIVERY MODE
			02/28/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/913,325

Applicant(s)

GLEAVE ET AL.

Examiner

Tracy Vivlemore

Art Unit

1635

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 03 January 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: 9, 11, 29, 30, 33 and 34.  
Claim(s) rejected: 6, 8, 10, 12-17, 31 and 32.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

TV  
February 20, 2007

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue the examiner has characterized the Sensibar reference as teaching gene therapy, but this reference does not deal with gene therapy and because the cells were first transfected to overexpress TRPM-2 there is no suggestion of a therapeutic use for reducing TRPM-2 expression. Applicants further argue Sensibar teaches increased TRPM-2 could protect from TNF alpha toxicity but there is no connection in the cited art between TNF-alpha and androgen withdrawal as described in Bruchovsky. The Sensibar reference is not relied upon to teach the idea of gene therapy, but to teach that antisense oligonucleotides targeted to TRPM-2, including the specific sequence of the instant claims, and their use to reduce TRPM-2 expression were known in the art prior to the time of invention. The only statement with regard to gene therapy made by the examiner in the context of the Sensibar reference is that antisense inhibition of gene expression is a type of gene therapy, something also recognized in the Bruchovsky reference in figure 9.

Applicants reiterate their argument that Bruchovsky does not provide a reasonable expectation of success because their teaching was merely a suggestion for future research and therefore nothing more than an invitation to experiment, which is not a valid basis for a finding of obviousness. As stated before, an obviousness rejection does not require that the outcome of an experiment be known. Bruchovsky explicitly suggests combining androgen withdrawal with TRPM-2 gene therapy in the form of antisense oligonucleotides and the further combination of gene therapy to other genes such as BCL-2. Applicants also reiterate the effect of TRPM-2 on apoptosis was unknown, citing this as an additional reason for no expectation of success, because it was unknown that decrease of TRPM-2 would lead to a therapeutic benefit. Applicants' focus on whether it was known if TRPM-2 affects apoptosis is not understood because the claims do not require TRPM-2 have such an effect and applicants have provided no reason why TRPM-2 must affect apoptosis in order to be beneficial in a therapy. The Bruchovsky reference explicitly suggests combining androgen withdrawal with antisense inhibition of TRPM-2 as a viable direction for future research, because both androgen withdrawal and antisense gene inhibition were known, the person of skill would have had a reasonable expectation of success in combining the two methods. Applicants' assertion that some of the examiner's statements seem contrary to the history of science cannot be answered because they are not relevant to the rejection of record.

In response to a previous action, applicants provided a declaration by one of the inventors describing an alleged synergistic effect of combining antisense and chemotherapeutic agents. In the final rejection the examiner stated the results described in the declaration were not commensurate in scope with the claimed method because the experiments described in the declaration did not have a step of androgen withdrawal. In response, applicants argue a step of androgen withdrawal is not necessary in a cell culture method as used in the experiments and is only relevant in an in vivo context. This argument supports the examiner's position because the experiments described in Dr. Gleave's declaration that are alleged to show synergy were in fact in vivo experiments to reduce tumor volume in mice and therefore the lack of an androgen withdrawal step is very relevant.

Applicants state the examiner's reliance on Raghavan reference is essentially an argument that once some combination is known all other combinations are obvious and further argues some suggestion of the claimed invention is required. The use of the Raghavan reference is not an "invitation to experiment", Raghavan specifically teaches chemotherapeutic agents are commonly used as treatment for prostate cancer and explicitly suggests its use in combination with other treatments, providing a suggestion to employ chemotherapeutic agents in combination with other therapies. Also, as noted in the final rejection, Raghavan does not provide the only teaching of combination therapies, Bruchovsky et al. also teach that combination therapies using cytotoxic agents were known in the art at the time of invention and also suggest their use in treatment of prostate cancer.



RICHARD SCHNIZER, PH.D.  
PRIMARY EXAMINER